Synthesis and characterization of new 1,3-Oxazepine-4,7-dione compounds from 1,2-diaminobenzene

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Abstract---In this research, done synthesized a series of new 1,3-oxazepine-4,7-dione derivatives as D1-D3 compounds via using [2+5] cycloaddition reaction. Synthesized compounds that have been bis azo groups [B1-B3] from 1,2-diaminobenzene via coupling its diazonium salt with phenoxide anion of 4-alkoxybenzaldehyde which Alkoxy was as pentyl, hexyl, and Heptyl groups. These compounds B1-B3 are condensed with 4-Bromoaniline in Schiff bases reactions to give bisazoimine derivatives C1-C3. The compounds C1-C3 were produced by cycloaddition reaction to produce 1,3-oxazepine-4,7-dione derivatives D1-D3. The structures of the synthesized compounds are characterized by spectroscopic methods, such as FTIR, and 1HNMRR spectra with the elemental composition analysis. The compounds D1-D3 that are synthesized play a big role in the inhibition of growth.

Keywords---1,3-oxazepine, Schiff bases syntheses, Cyclo addition, biological activity.
**Introduction**

Azo compound, any organic compound, diverse set of both natural and synthetic molecules containing at least one double-bonded nitrogen group. Though there is an extremely wide range of azo compounds, the most common are pigments and dyes (Aljamali, 2015). Oxazepine is a heterocyclic molecule that consists of a seven-membered ring and includes oxygen and nitrogen atoms (Prakash et al., 2021). The biological activity of oxazepine compounds include anticonvulsant (Sharma et al., 2008), antiviral (Campiani et al., 1996), antifungal (Kumar & Joshi, 2009), and other uses in many applications. Cycloaddition reaction is the kind of reaction used in the production of the 1,3-oxazepine chemical ring classed as (2+5) to create seven cycloaddition reactions. Two imine groups were added to a five-membered component, such as phthalic anhydrides, to form a heterocycle with seven members (Carruthers, 2013; Jørgensen, 2002). The antibacterial and antiviral functions of a molecule are entirely dependent on chemicals that target viruses and bacteria biologically, limit their rate of growth, and are damaging to injured tissue. Recently produced antibacterial agents include natural compounds that have been chemically modified (Aftan et al., 2021; Kanichar et al., 2014).

**Experimental Part**

**Characterization**

The FTIR spectra use an FT-IR instrument that has model 8300 Shimadzu. 1H NMR spectra that were used Brüker ACF 400 spectrometer. The chemicals used were obtained from different such as, Fluka, BDH, and Merck companies.
Scheme 1. Synthesis of substituted 1,3-oxazepine-4,5-dione D1-D3.

General procedure for the synthesis of Azo compounds (B1-B3)

In cooling bath, added %10 HCl solution (5 mL) to 1,2-diaminobenzene (0.01 mol) then add (2-3) drops of Conc. HCl into test tube No.1. On the other hand, prepare NaNO$_2$ (0.02 mole, 1.379 g) in distilled water (5 mL) in test tube No.2. When the
temperature of the solution in test tube No. 1 became (0-5 ‘C), added test tube No. 2 to test tube No.1. Prepare each solution 4-pentoxybenzaldehyde as R1 (0.02 mole), 0.02 mole 4-hexoxylbenzaldehyde R2, 0.02 mole 4-heptoxybenzaldehyde R3, in (10 ml) %10 NaOH into test tube No.3. Finally, added the mixture of solutions into test tube No. 3 (Zhang et al., 2020). Then filtration of the solution, and collected the precipitate.

**General procedure for the synthesis of Schiff's base compounds (C1-C3) (Ye et al., 2018).**

(2-3) drops of glacial acetic acid were added to each compound (B1-B3) (0.01 mol), then mixture with 4-bromoaniline (0.02 mole) in a solvent, such as 20 ml of EtOH. Refluxed the mixture of solution for 3 hours. Finally, the precipitates were formed, collected by filtration, dried, and recrystallized. Listed in Table 1.

<table>
<thead>
<tr>
<th>ComP. No.</th>
<th>Yield %</th>
<th>Colour</th>
<th>m.p. °C</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1</td>
<td>67</td>
<td>Brown</td>
<td>165-170</td>
</tr>
<tr>
<td>C2</td>
<td>66</td>
<td>Brown</td>
<td>168-172</td>
</tr>
<tr>
<td>C3</td>
<td>70</td>
<td>Dark brown</td>
<td>166-171</td>
</tr>
</tbody>
</table>

**General procedure for the synthesis of Oxazepine compounds (D1-D3) (Alfatlawi et al., 2018; Ayfan et al., 2019)**

The mixture of each Schiff`s bases (C1-C3) (0.01mol) with 0.02-mole phthalic anhydride in 20 ml of dry benzene. Then, refluxed the mixture. Finally, filtration of solution and collected the precipitate and recrystallized via dry 1,4-dioxan.

<table>
<thead>
<tr>
<th>ComP. No.</th>
<th>Yield %</th>
<th>Colour</th>
<th>m.p. °C</th>
</tr>
</thead>
<tbody>
<tr>
<td>D1</td>
<td>69</td>
<td>Light brown</td>
<td>230-235</td>
</tr>
<tr>
<td>D2</td>
<td>63</td>
<td>Brown</td>
<td>228-232</td>
</tr>
<tr>
<td>D3</td>
<td>68</td>
<td>Brown</td>
<td>219-224</td>
</tr>
</tbody>
</table>

**Results and Discussion**

The compounds 4-Alkoxylbenzaldehyde as start materials were prepared from the reaction of 4-hydroxybenzaldehyde with appropriate alkyl halides (1-Bromo pentane and 1-Bromo hexane, 1-Bromo heptane) (Sleevi et al., 1991). The azo compounds form from a diazonium salt and a coupling component. The aryl diazonium ion is directed to the meta position with respect to the carbonyl group and ortho site with respect to the alkoxy group (Du & Huang, 2019). The titled compounds were synthesized from the reaction of previously synthesized compounds (B1 - B3) with 4-Bromoaniline through the condensation reaction.
FT-IR spectra for compounds C1-C3 showed in Figures (1, 3) the disappearance of the -NH$_2$ group and on other hand the appearance of a new imine group in the range (1636 - 1642 cm$^{-1}$) (Nolte et al., 2021). The bands at the range (3062 – 3081 cm$^{-1}$) for the C–H aromatic stretching, (2984 – 2870 cm$^{-1}$) for asymmetrical and symmetrical C–H aliphatic stretching, while the azo groups appeared at (1541-1453 cm$^{-1}$) and bands at (1593-1606 cm$^{-1}$) returned to C = C aromatic stretching (Ozaki et al., 2021).

Figure 1. FT-IR spectra of compound C1.

Figure 2. FT-IR spectra of compound C2.
The structure of this group was identified by using $^1$HNMR spectroscopy. The $^1$HNMR spectrum of compound C3 is shown in Figure 5, the proton of the imine group CH=N (2H) generates a signal at 8.37 ppm, and the aromatic protons generate signals at 6.52 – 8.17 ppm (Mandal & Paul, 2022). At 1.04 - 1.06, six protons showed as a triplet, which could be referred to –CH$_3$, and 20 protons appeared as a multiplet, which could be referred to –CH$_2$- CH$_2$. At 3.32-4.06 (4H), the –OCH$_2$ groups of the heptyl group appeared as a triplet (Roduner et al., 2019).

The synthesized compounds of Oxazepine produce via Schiff’s base compounds that reacted with phthalic anhydride (Jabar et al., 2020). Figures 6 showed absorption bands at (1722-1731) cm$^{-1}$ that returned to (C=O of lactone stretching), (1664-1668) cm$^{-1}$, and (C=O of lactam stretching) (Zhang et al., 2020). The bands at (3078-3140) cm$^{-1}$ that for (C– H) of the aromatic ring, then (2897-
2976 cm\(^{-1}\) for (\(\nu\) C–H) of aliphatic chain, (1510-1524) cm\(^{-1}\) (\(\nu\) N=N) (Sallal & Ghanem, 2018).

Figure 5. FT-IR spectra of compound D1

Figure 6. FT-IR spectra of compound D2.
1HNMR spectroscopy was used to confirm the structure of these compounds. Figure 8 shows the 1HNMR spectrum of compound D1, the following characteristic chemical shifts (d6 -DMSO, ppm) appeared: signal observed at δ 6.9 – 7.4 ppm (18H). Four protons appeared as a doublet at δ 8.1 ppm. Six protons appeared as a triplet at δ 0.93-0.95 which could be assigned to –CH₃, protons appeared as a multiple at δ 1.6-1.9 ppm which could be assigned to (-CH₂)₆ (24 H). The -OCH₂ groups of pentyl substituent appeared as a triplet at δ 3.80-3.83 ppm (Alfatlawi et al., 2018).

Table 3
Elemental composition analysis for compounds D1-D3.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Measured % (Calculated; %)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>C</td>
</tr>
<tr>
<td>D1</td>
<td>62.52(62.46)</td>
</tr>
</tbody>
</table>
As seen in Figure 9, the EDX mapping of compounds D1-D3 including additives reveals the distribution and relative abundance of atoms within the mixes. The Figures clearly depict the uniform distribution of components inside these complexes. Bromine and carbon atoms are numerous and widely dispersed throughout the mixtures. In addition, the photos suggest that these molecules include additional elements (nitrogen and oxygen) (Scimeca et al., 2018).

Figure 9. EDX mapping for 1,3-Oxazepine-4,5-dione compounds.

Oxazepine particle shape and size, amount of cross-sectioning, and homogeneity may be determined using FESEM analysis (Xie et al., 2007). FESEM images suggest that Oxazepine compounds are extremely homogenous and have relatively smooth surfaces, as shown in Figure 10.
Biological activity

The synthesized compounds were tested against different types of gram-positive bacteria such as *Staphylococcus aureus*, in addition to gram-negative bacteria such as *Escherichia coli* and *Bacillus*. The compounds D1-D3 were used at a concentration of 10, 50, and 100 μg/ML via used the agar diffusion method (De et al., 2019). The results are shown in Table 4.

Table 4
Antibacterial activities of the compounds (D1-D3).

<table>
<thead>
<tr>
<th>Sample</th>
<th>Staphylococcus aureus</th>
<th>Escherichia coli</th>
<th>Bacillus</th>
</tr>
</thead>
<tbody>
<tr>
<td>D1</td>
<td>++</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>D2</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>D3</td>
<td>-</td>
<td>++</td>
<td>+</td>
</tr>
</tbody>
</table>

Note: (-) = No inhibition, (+) =10-14 mm, (++): 15-22 mm.

Conclusions

In conclusion, we have synthesized a series of new 1,3-oxazepine-4,7-dione derivatives using a Schiff’s bases synthesis. In addition, all newly synthesized 1,3-oxazepine-4,7-dione were tested as antibacterial via the use of different types of bacteria such as *Staphylococcus aureus, escherichia coli, and bacillus*, these compounds that synthesized play a big role as an inhibition for growth of these bacterial via used different concentrations of Oxazepine compounds D1-D3.
References


